

Substitute for form 1449A/PTO			Complete if Known		
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)			Application Number	10/564,945	
			Filing Date	January 9, 2006	
			First Named Inventor	Katherine Weibaecher	
			Art Unit	1614	
			Examiner Name		
Sheet 1	of 6		Attorney Docket Number	60005161-0217	
U.S. PATENT DOCUMENTS					
Examiner Initials*	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
	1	6,579,675	06-17-2003	Kamb	
	2	6,552,079	04-22-2003	Scarborough et al.	
	3	6,548,517	04-15-2003	Marlowe et al.	
	4	6,528,534	03-04-2003	Fisher et al.	
	5	6,521,593	02-18-2003	Laug	
	6	6,399,627	06-04-2002	Song et al.	
	7	6,291,469	09-18-2001	Fisher et al.	
	8	6,245,809	06-12-2001	Scarborough et al.	
	9	6,037,176	03-14-2000	Bennett et al.	
	10	5,968,902	10-19-1999	Scarborough et al.	
	11	5,958,732	09-28-1999	Scarborough et al.	
	12	5,935,926	08-10-1999	Scarborough et al.	
	13	5,843,897	12-01-1998	Scarborough et al.	
	14	5,807,825	09-15-1998	Scarborough et al.	
	15	5,786,333	07-28-1998	Scarborough et al.	
	16	5,770,564	06-23-1998	Scarborough et al.	
	17	5,759,999	06-02-1998	Scarborough et al.	
	18	5,756,451	05-26-1998	Scarborough et al.	
	19	5,736,339	04-07-1998	Scarborough et al.	
	20	5,686,571	11-11-1997	Scarborough et al.	
	21	5,686,570	11-11-1997	Scarborough et al.	
	22	5,686,569	11-11-1997	Scarborough et al.	
	23	5,686,568	11-11-1997	Scarborough et al.	
	24	5,686,567	11-11-1997	Scarborough et al.	
	25	5,686,566	11-11-1997	Scarborough et al.	
	26	5,652,110	07-29-1997	Kim et al.	
	27	5,652,109	07-29-1997	Kim et al.	
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Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known		
Sheet 2 of 6		Application Number 10/564,945		Filing Date January 9, 2006		
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Examiner Initials*	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	
	28	5,578,704	11-26-1996	Kim et al.		
	29	5,496,724	03-05-1996	Scarborough et al.		
	30	5,344,783	09-06-1994	Scarborough et al.		
	31	5,318,899	06-07-1994	Scarborough et al.		
	32	5,262,319	11-16-1993	Iwata et al.		
FOREIGN PATENT DOCUMENTS						
Examiner Initials*	Cite No. ¹	Foreign Patent Number <small>Country Code² Number³ Kind Code⁴ (if known)</small>	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T 6
	33	V/O 97/48444	12-24-1997	Becton Dickinson & Co.		<input type="checkbox"/>
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OTHER ITEMS – NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	34	Amirkhosravi, A., Amaya, M. & Siddiqui, F.A. Blockade of GpIIb/IIIa inhibits the release of vascular endothelial growth factor (VEGF) from tumor cell-activated platelets and experimental metastasis. Platelets 10, 285-292 (1999).	
	35	Arguello, F., Baggs, R.B. & Frantz, C.N. A murine model of experimental metastasis to bone and bone marrow. Cancer Res 48, 6876-81 (1988).	
	36	Bakewell SJ, et al., Platelet and osteoclast beta3 integrins are critical for bone metastasis. Proc Natl Acad Sci USA (2003 Nov 25) 100(24):14205-10.	
	37	Body, J.J. et al. A phase I study of AMG-0007, a recombinant osteoprotegerin construct, in patients with multiple myeloma or breast carcinoma related bone metastases. Cancer 97, 887-92 (2003).	
	38	Borsig, L., Wong, R., Hynes, R.O., Varki, N.M. & Varki, A. Synergistic effects of L- and P-selectin in facilitating tumor metastasis can involve non-mucin ligands and implicate leukocytes as enhancers of metastasis. Proc Natl Acad Sci U S A 99, 2193-8 (2002).	
	39	Brooks, P.C., Clark, R.A. & Cheresh, D.A. Requirement of vascular integrin alpha v beta 3 for angiogenesis. Science 264, 569-71 (1994).	
	40	Chen, Y.P. et al. Ser-752-->Pro mutation in the cytoplasmic domain of integrin beta 3 subunit and defective activation of platelet integrin alpha IIb beta 3 (glycoprotein IIb-IIIa) in a variant of Glanzmann thrombasthenia. Proc Natl Acad Sci U S A 89, 10169-73 (1992).	
	41	Clemetson et al. Cell. Mol. Life Sci. 54, 502-513 (1998).	
	42	Clohisy, D.R. & Ramnaraine, M.L. Osteoclasts are required for bone tumors to grow and destroy bone. J Orthop Res 16, 660-6 (1998).	
	43	Coleman, R.E. Future directions in the treatment and prevention of bone metastases. Am J Clin Oncol 25, S32-8 (2002).	
	44	Engelman, V.W. A peptidomimetic antagonists of the avb3 integrin inhibits bone resorption in vitro and prevents osteoporosis in vivo. Journal of Clinical Investigation 99, 2284-2292 (1997).	
	45	Felding-Habermann, B., Habermann, R., Saldivar, E. & Ruggeri, Z.M. Role of beta3 integrins in melanoma cell adhesion to activated platelets under flow. J Biol Chem 271, 5892-900 (1996).	
	46	Felding-Habermann, B. et al. Integrin activation controls metastasis in human breast cancer. Proc Natl Acad Sci U S A 98, 1853-8 (2001).	

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¹ Applicant's unique citation designation number (optional). ² Applicant is to place a check mark here if English language Translation is attached.

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Sheet	4	of	6	Attorney Docket Number	60005161-0217
	47	Feng, X. et al. A Glanzmann's mutation in beta 3 integrin specifically impairs osteoclast function. J Clin Invest 107, 1137-44 (2001).			
	48	Fitzgerald, L.A. et al. Anal. Biochem 151, 169-177 (1985).			
	49	Francis, J.L. & Amirkhosravi, A. Effect of antihemostatic agents on experimental tumor dissemination. Semin Thromb Hemost 28, 29-38 (2002).			
	50	Gasic, G.J., Gasic, T.B. & Stewart, C.C. Antimetastatic effects associated with platelet reduction. Proc Natl Acad Sci U S A 61, 46-52 (1968).			
	51	Guise, T.A. et al. Evidence for a causal role of parathyroid hormone-related protein in the pathogenesis of human breast cancer-mediated osteolysis. J Clin Invest 98, 1544-9 (1996).			
	52	Hodivala-Dilke, K.M. et al. Beta3-integrin-deficient mice are a model for Glanzmann thrombasthenia showing placental defects and reduced survival. J Clin Invest 103, 229-38 (1999).			
	53	Honore, P. et al. Osteoprotegerin blocks bone cancer-induced skeletal destruction, skeletal pain and pain-related neurochemical reorganization of the spinal cord. Nat Med 6, 521-8 (2000).			
	54	Hood, J.D. & Cheresh, D.A. Role of integrins in cell invasion and migration. Nat Rev Cancer 2, 91-100 (2002).			
	55	Horton, M.A., Taylor, M.L., Arnett, T.R. & Helfrich, M.H. Arg-Gly-Asp (RGD) peptides and the anti-vitronectin receptor antibody 23C6 inhibit dentine resorption and cell spreading by osteoclasts. Exp Cell Res 195, 368-75 (1991).			
	56	Hynes, R.O. Integrins: versatility, modulation, and signaling in cell adhesion. Cell 69, 11-25 (1992).			
	57	Ichinohe, T. et al. Collagen-stimulated activation of Syk but not c-Src is severely compromised in human platelets lacking membrane glycoprotein VI. J Biol Chem 272, 63-8 (1997).			
	58	Inoue, M., Namba, N., Chappel, J., Teitelbaum, S.L. & Ross, F.P. Granulocyte macrophage-colony stimulating factor reciprocally regulates alphav-associated integrins on murine osteoclast precursors. Mol Endocrinol 12, 1955-62 (1998).			
	59	Kaplan, I.D., Valdagni, R., Cox, R.S. & Bagshaw, M.A. Reduction of spinal metastases after preemptive irradiation in prostatic cancer. International Journal of Radiation and Oncological Biology and Physiology 18, 1019-1025 (1990).			
	60	Karparkin, S., Pearlstein, E., Ambrogio, C. & Collier, B.S. Role of adhesive proteins in platelet tumor interaction in vitro and metastasis formation in vivo. J Clin Invest 81, 1012-9 (1988).			
	61	Law, D.A. et al. Integrin cytoplasmic tyrosine motif is required for outside-in alphab1bbeta3 signalling and platelet function. Nature 401, 808-11 (1999).			
	62	Lipton, A. et al. Pamidronate prevents skeletal complications and is effective palliative treatment in women with breast carcinoma and osteolytic bone metastases: long term follow-up of two randomized, placebo-controlled trials. Cancer 88, 1082-90 (2000).			
	63	Marshall. Solid oral dosage forms. Modern Pharmaceutics 7, 359-427 (1979).			

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64	McHugh, K.P. Mice lacking b3 integrins are osteosclerotic because of dysfunctional osteoclasts. Journal of Clinical Investigation 105, 433-440 (2000).
65	Mundy, G.R. Metastasis to bone: causes, consequences and therapeutic opportunities. Nat Rev Cancer 2, 584-93 (2002).
66	Parfitt, A.M. Bone histomorphometry: Standardization of nomenclature, symbols, and units. Report of the ASBMR histomorphometry of nomenclature committee. Journal of Bone Mineral Research 2, 595-610 (1987).
67	Pearlsstein, E., Ambrogio, C. & Karparkin, S. Effect of antiplatelet antibody on the development of pulmonary metastases following injection of CT26 colon adenocarcinoma, Lewis lung carcinoma, and B16 amelanotic melanoma tumor cells into mice. Cancer Res 44, 3884-7 (1984).
68	Phillips, D.R., Charo, I.F. & Scarborough, R.M. GPIIb-IIIa: the responsive integrin. Cell 65, 359-62 (1991).
69	Reynolds, L.E. et al. Enhanced pathological angiogenesis in mice lacking beta3 integrin or beta3 and beta5 integrins. Nat Med 8, 27-34 (2002).
70	Reynolds, A. et al. Rational siRNA design for RNA interference. Nature Biotechnology 22 (2004).
71	Rodan, S.B. & Rodan, G.A. Integrin function in osteoclasts. J Endocrinol 154 Suppl, S47-56 (1997).
72	Rosen, L.S. Efficacy and safety of zoledronic acid in the treatment of bone metastases associated with lung cancer and other solid tumors. Semin Oncol 29, 28-32 (2002).
73	Ross, F.P. et al. Interactions between the bone matrix proteins osteopontin and bone sialoprotein and the osteoclast integrin alpha v beta 3 potentiate bone resorption. J Biol Chem 268, 9901-7 (1993).
74	Saad, F. Treatment of bone complications in advanced prostate cancer: rationale for bisphosphonate use and results of a phase III trial with zoledronic acid. Semin Oncol 29, 19-27 (2002).
75	Silletti, S., Kessler, T., Goldberg, J., Boger, D.L. & Cheresh, D.A. Disruption of matrix metalloproteinase 2 binding to integrin alpha v beta 3 by an organic molecule inhibits angiogenesis and tumor growth in vivo. Proc Natl Acad Sci U S A 98, 119-24 (2001).
76	Smith, J.W. J. Biol. Chem. 263, 18726-18731 (1988).
77	Soriano, P., Montgomery, C., Geske, R. & Bradley, A. Targeted disruption of the c-src proto-oncogene leads to osteopetrosis in mice. Cell 64, 693-702 (1991).
78	Stalano, N. et al. Echistatin inhibits the adhesion of murine melanoma cells to extracellular matrix components. Biochem Mol Biol Int 35, 11-9 (1995).
79	Tanaka, S. et al. c-Cbl is downstream of c-Src in a signalling pathway necessary for bone resorption. Nature 383, 528-31 (1996).
80	Teti, A., Migliaccio, S. & Baron, R. The role of the alphaVbeta3 integrin in the development of osteolytic bone metastases: a pharmacological target for alternative therapy? Calcif Tissue Int 71, 293-9 (2002).
81	Trikha et al. Cancer Res. 56, 5071-5078 (1996).

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**INFORMATION DISCLOSURE
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| 82 | Weilbaecher, K.N. et al. Linkage of M-CSF signaling to Mltf, TFE3, and the osteoclast defect in Mltf(mi/mi) mice. Mol Cell 8, 749-58 (2001). |
| 83 | Wu, Y. et al. Differential activation and redistribution of c-Src and Fyn in platelets, assessed by MoAb specific for C-terminal tyrosine-dephosphorylated c-Src and Fyn. Biochim Biophys Acta 1497, 27-36 (2000). |
| 84 | Yoneda, T. et al. Actions of bisphosphonate on bone metastasis in animal models of breast carcinoma. Cancer 88, 2979-88 (2000). |
| 85 | Zhang, J. et al. Osteoprotegerin inhibits prostate cancer-induced osteoclastogenesis and prevents prostate tumor growth in the bone. J Clin Invest 107, 1235-44 (2001). |

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Signature

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